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09/668,508	09/22/2000	Henry E. Young	1304-1-019CIP	1973

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EXAMINER
TON, THALAN N

ART UNIT PAPER NUMBER

1632

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/668,508

Applicant(s)

YOUNG ET AL.

Examiner

Thaia N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 September 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 4,6,7 and 18-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5 and 8-17 is/are rejected.
- 7) ☒ Claim(s) 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-32 are currently pending. Claims 1-3, 5, 8-17 are under current examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-3, 5, 8-17 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the requirement for restriction should be reconsidered or modified by consolidation rather than expansion of the number of claim groups provided, and further that the conjoint examination and inclusion of all of the present claims in the present Application would not present an undue burden on the Examiner as the relevant prior art for the most part, should be commonly classified and consequently found [see p. 2 of Applicants' Response]. This is not found persuasive because the inventions in Groups I-VII have acquired a separate status in the art as a separate subject for inventive effort and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4, 6, 7, 18-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claim Objections

Claim 15 is objected to because of the following informalities: the claim recites "likestem" in line 2 of the claim. It appears that the claim should read "like stem". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 8-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 8, 11, 12 and 15 as written, are vague. The claims recite a pluripotent "embryonic-like" stem cell. Although the specification states that these cells are derived from non-embryonic or post-natal animal cells or tissues, it is unclear how these cells are "embryonic-like". Claims 2, 3, 5 and 14 depend from claim 1, claims 9 and 10 depend from claim 8, claim 13 depends from claim 12, claims 16 and 17 depend from claim 15.

Claims 1 and 8 recite that the pluripotent embryonic-like stem cell is "derived from". However, it is unclear what the metes and bounds of the term "derived" are. For example, although the origin of the cells is from non-embryonic or postnatal animal cells or tissue, are the cells altered such that they are different from the cells that they are originally derived from? Claims 2, 3, 5, and 14 depend from claim 1, claims 9 and 10 depend from claim 8.

Claim 5, as written, is unclear. The claim recites that the pluripotent mesenchymal stem cells is "derived from" the cell of claim 1. It is unclear what the term "derived from" encompasses. Are these cells altered from the cells of claim 1? Clarification and/or amendment is requested.

Claim 11, as written, is unclear. The claim recites freezing cells and then culturing the cells. It is unclear how cells can be cultured after freezing. Furthermore, the claim is incomplete because it is unclear how culturing cells in part (c) of the claim relates to the preamble, "A method of isolating a pluripotent embryonic-like stem cell".

Claim 12, as written, is unclear. The claim recites slow freezing of the cells in part (b) of the claim and then culturing of the cells in part (c) of the claim. It is unclear how cells that are at a final temperature of -80 C would be subsequently cultured. Furthermore, the claim is incomplete because it is unclear how propagating cultures having a single cell in part (e) of the claim relates to the preamble, A method of isolating a clonal pluripotent embryonic-like stem cell line.

Claim 13, as written, is unclear. The claim recites that the stem cell line is "developed" by the method of claim 12, however, it is unclear how the stem cell line would be "developed", nor is it clear what the metes and bounds of this term are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 8, 9 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Shambloot *et al.* [PNAS, 95:13726-13731, 1998]

The claims are directed to pluripotent embryonic-like stem cells, pluripotent mesenchymal stem cells, and cultures comprising the pluripotent embryonic-like stem cells. Note that claim 13 is a product by process claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products

or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Shamblott *et al.* teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells [PGCs] and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers [see *Abstract*]. In particular, Shamblott *et al.* teach that gonadal ridges and mesenteries of 5 to 9 week old human fetuses and cells initially cultured on a layer of mouse STO fibroblast feeder layer. The cells formed embryoid bodies, which were collected and analyzed immunohistochemically [see pp. 13726-13727, *Materials & Methods*]. It was found that the embryoid bodies demonstrated derivatives of the three embryonic germ layers [see p. 13729, 2nd column and Table 1]. Note that the claims are directed to pluripotent cells derived from non-embryonic tissues, as such, the fetal tissue described by Shamblott *et al.* teach this requirement.

Accordingly, Shamblott *et al.* anticipate the claimed invention.

Claims 1-3, 5, 8-10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Pittenger *et al.* [*Science*, 284:143-147, 2 April 1999].

The claims are directed to pluripotent human embryonic-like stem cells derived from non-embryonic or postnatal animal cells or tissue, pluripotent mesenchymal stem cells and cultures comprising the pluripotent embryonic-like stem cells. Note that claim 13 is a product-by-process claim [see *supra*].

Pittenger teach human mesenchymal stem cells isolated from adult bone marrow which are found to differentiate into multiple mesenchymal lineages *in vitro* [see p. 143, 2nd column, 1st full paragraph]. Pittenger teach that these mesenchymal cells were characterized by their ability to proliferate in culture [see Figure 1]. Pittenger teach that the differentiation potential of the mesenchymal stem cells was tested by specific differentiation in adipogenic differentiation, chondrogenic differentiation and osteogenic differentiation under specific conditions [see pp. 144-145].

Accordingly, Pittenger anticipate the claimed invention.

Claims 1, 3, 5, 8, 9, 13 are rejected under 35 U.S.C. 102(b) as being anticipate by Prockop [*Science*, 276:71-74, 1997].

Prockop teaches the isolation of marrow stromal cells from mouse bone marrow which can be differentiated *in vitro* into osteoblasts, chondrocytes, adipocytes [see *Abstract* and p. 72, 2nd column, 1st paragraph].

Accordingly, Prockop anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger *et al.* [Science, 284:143-147, 2 April 1999] when taken with Spector *et al.* [Cells A Laboratory Manual, Vol. 1, pp. 2.12-2.13].

Pittenger teach human mesenchymal stem cells isolated from adult bone marrow which are found to differentiate into multiple mesenchymal lineages *in vitro* [see p. 143, 2nd column, 1st full paragraph]. Pittenger teach that these mesenchymal cells were characterized by their ability to proliferate in culture [see Figure 1]. Pittenger teach that the differentiation potential of the mesenchymal stem cells was tested by specific differentiation in adipogenic differentiation, chondrogenic differentiation and osteogenic differentiation under specific conditions [see pp. 144-145]. They differ from the claimed invention in that they do not teach the slow freezing of the cells in a medium containing 7.5% (v/v) dimethyl sulfoxide until a final temperature of -80°C and then subsequently culturing the cells.

However, prior to the time the claimed invention was made, Spector teach the freezing of cells to a final temperature of -80°C [see p. 2.12] using DMSO in a range from 5-20% [see p. 2.13, Notes], and the subsequent thawing and culturing of the frozen cells [see p. 2.13]. Accordingly, in view of the combined teachings of Pittenger and Spector, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to freeze the cells, as taught by Pittenger, using the methods taught by Spector. One of skill in the art would have been sufficiently motivated to use the method taught by Spector because it provides a way to preserve a cell source indefinitely.

Thus the claimed invention as a whole was clearly *prima facie* obvious at the time the claimed invention was made especially in the absence of sufficient, clear and convincing evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger *et al.* [Science, 284:143-147, 2 April 1999] in view of Sambrook *et al.* [Molecular Cloning, Book 3, 1989].

Pittenger teach human mesenchymal stem cells isolated from adult bone marrow which are found to differentiate into multiple mesenchymal lineages *in vitro* [see p. 143, 2nd column, 1st full paragraph]. Pittenger teach that these mesenchymal cells were characterized by their ability to proliferate in culture [see Figure 1]. Pittenger teach that the differentiation potential of the mesenchymal stem cells was tested by specific differentiation in adipogenic differentiation, chondrogenic differentiation and osteogenic differentiation under specific conditions [see pp. 144-145]. They differ from the claimed invention in that they do not teach transfecting the pluripotent embryonic stem-like stem cells with a DNA construct comprising at least one of a marker gene or a gene of interest.

However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Pittenger and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed

invention was made, to use the mesenchymal stem cells, as taught by Pittenger and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus the claimed invention as a whole was clearly *prima facie* obvious at the time the claimed invention was made especially in the absence of sufficient, clear and convincing evidence to the contrary.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Patsy Zimmerman, Patent Analyst, at (703) 305-2758. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703)872-9306.

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